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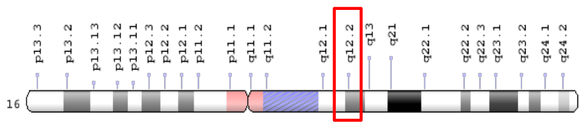
Analysis of the FTO Gene and its Association with Obesity

Objective

The objective of this study is to understand the function of the Fat Mass and Obesity associated gene (FTO gene) and its effect on the predisposition for obesity in humans. There is a current lack of scientific knowledge about the exact causes of obesity, however, the FTO gene has a strong correlation to obesity. This project will allow for a better understanding about how genes can affect body composition and inform future studies. In addition, the more we can learn about the FTO gene and its association with obesity, the more we can research new treatment options and ways to prevent obesity.

Background

- Obesity is one of the greatest health concerns worldwide and has tripled since the 1970s.
- The World Health Organization has estimated that 1.2 billion adults were overweight and 680 million adults were obese in 2016.
- The FTO gene can be found on the chromosome 16 of the long arm at 16q12.2, this is the exact locus on the chromosome.



- The FTO gene contains an associated protein called alpha-ketoglutarate-dependent dioxygenase. This protein regulates thermogenesis (production of heat) in the body and controls the adipocyte differentiation of brown and white fat cells in the body.
- Due to the alpha-ketoglutarate-dependent dioxygenase protein association in the FTO gene, the FTO gene directly affects how the body decides to use energy in the body. A mutation in the FTO gene can cause the body to produce more white fat cells then normal.
- A functions of white fat cells is to store energy for the body instead of using the energy as fuel. This increase in white fat cells in the body can result in an increased predisposition for obesity.
- It has been discovered that on the FTO gene SNPs variant rs9939609 the genotype was discovered to be TT, AT and AA.
- Based on a Romanian cohort study, participants who had the genotype AA had higher BMI then those with a TT genotype.

Table 1

Differences between the 3 FTO genotypes and Clinical/ paraclinical parameters and obesity associated disorders

MEASURE	**HmWt** (15/53, 28.3%)	**Ht** (20/53, 37.74%)	**HmMut** (18/53, 33.96%)	**P value ANOVA**
Weight (kg)	60.20 ± 15.76 (36.00 – 87.00)	81.40 ± 28.52 (35.00 – 130.00)	112.28 ± 35.16 (65.0 – 191.0)	**0.000**
Abdominal circumrence (cm)	77.27 ± 11.63 (62.00 – 107.0)	95.45 ± 30.13 (59.00 – 199.00)	111.67 ± 30.01 (68.0 – 180.0)	**0.002**
BMI (kg/cm2)	23.37 ± 3.98 (19.20 – 32.70)	30.33 ± 7.52 (20.03 – 45.90)	37.88 ± 9.43 (21.90 – 55.10)	**0.000**
Obesity (N)* (34/53, 65.15%)	3/15, 20 %	14/20, 70 %	17/18, 94.44 %	**0.000**

- The A-Allele seems to be the risk allele that has the strongest correlation to obesity and a higher BMI.

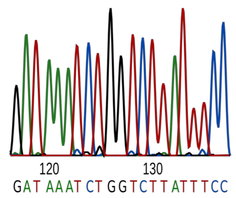
Methods

Procedures and Methods:

The key focus of this project is to research the FTO gene and its role in obesity. A small component of this project will be to analyze my own DNA sample and compare it with current research.

Laboratory Portion

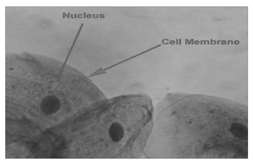
1. Obtain human chromosome 16 DNA sequence from GenBank.



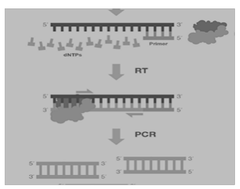
2. Design a PCR primer pair to amplify the intron region of the FTO gene containing SNP (rs 9939609) using the SnapGene software program.

SnapGene®
Software for molecular biology

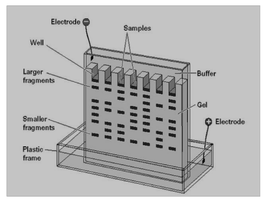
3. Extract genomic DNA from cheek cells for PCR amplification.



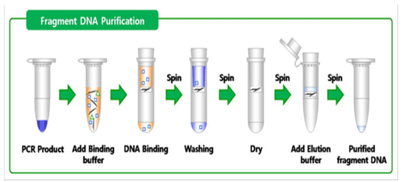
4. Conduct PCR, using the primers created to amplify FTO gene containing SNP (rs 9939609)



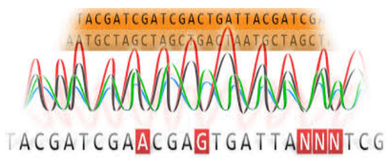
5. Analyze amplified DNA region by agarose gel electrophoresis. Electrophoresis is the process of separating DNA based on the size.



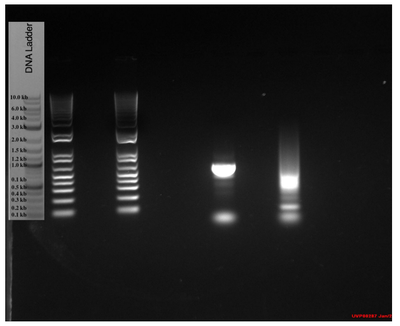
6. Clean PCR product and submit for sequencing.



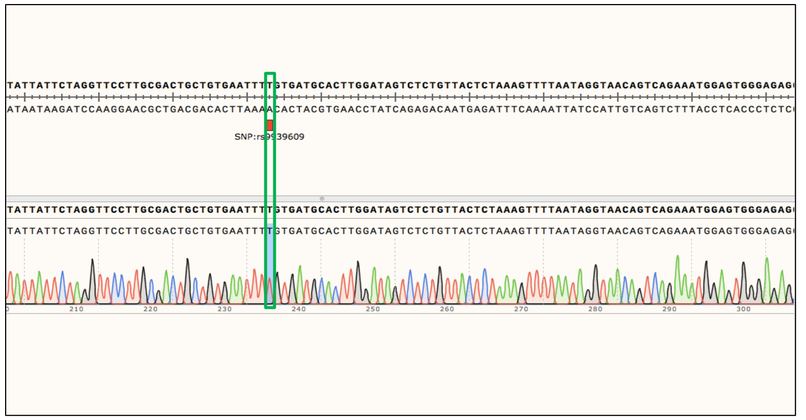
7. Align my sequence with the reference sequence from NCBI GenBank and analyze my sequence for SNP (rs 9939609).



Results



By analyzing the agarose gel, it was clear that the primers did not yield the expected control bands for FTO gene SNP rs 9939609. It was inferred there must have been an error in calculating the volume of template used, a loading error in the gel wells, or a malfunction in the primers itself. Although there are two fragments lines present, we lack one band line that was considered the control band. Due to the lack of reliability with the control, we could not confirm the experimental results.



The align sequence can be compared to the reference sequence to determine the FTO gene SNP rs 9939609 results above. The top sequence is the DNA sequence that was analyzed from the PCR amplification. Looking at the results of the SNP rs 9939609, it shows the risk allele is present with the alleles of TA. The bottom sequence, reference sequence from the NCBI GenBank, is the control FTO gene SNP rs 9939609 sequence which shows it has two non risk alleles of TT. Concluding from the results, the sequence with the TA alleles, shows a predisposition to obesity.

Discussion

By analyzing the FTO gene, scientists have a better understanding about how the body regulates itself. Because some people are genetically predisposed to having a higher chance of being obese, understanding how genetics plays a role in obesity will allow future scientists to conduct new studies to find new treatments or preventative measures for those with the FTO gene. If more people understood human genetics and its impact on body composition, more precautions can be taken to prevent obesity. Through this study, I hope to broaden people's mind about the increasing obesity epidemic and how genetics play a key role. Future studies can use genetic information like this to help create better obesity prevention strategies.

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